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THE EFFECT OF BEDREST ON VARIOUS PARAMETERS OF PHYSIOLOGICAL FUNCTION

Part XIII — A Review of Possible Mechanisms of Orthostatic Intolerance to Passive Tilt

by F. B. Vogt, W. A. Spencer, D. Cardus, and C. Vallbona

Prepared under Contract No. NAS 9-1461 *by*
TEXAS INSTITUTE FOR REHABILITATION AND RESEARCH
Houston, Texas
for Manned Spacecraft Center

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ABSTRACT

The review includes a discussion on bedrest and water immersion studies and relates the observations which have been reported in the literature on certain features of cardiovascular function, intravascular volume, and transfer of fluid and electrolytes into and out of the intravascular system to define a possible mechanism accounting for some features of "cardiovascular deconditioning" manifested in the passive tilt procedure. Experimental procedures are suggested which would test the validity of this hypothesis. It is concluded that future bedrest studies should be directed to defining more precisely the mechanism involved to account for the changes in tilt response after bedrest compared to those observed before bedrest.

FOREWORD

This study is part of a NASA investigation of the effect of bedrest on various parameters of physiological function. It was sponsored by NASA Manned Spacecraft Center under Contract NAS 9-1461, with Dr. Lawrence F. Dietlein, Chief, Space Medicine Branch, serving as Technical Monitor.

The authors are affiliated with Baylor University College of Medicine and the Texas Institute for Rehabilitation and Research as follows: Dr. Vogt, Department of Rehabilitation; Dr. Spencer, Department of Rehabilitation; Dr. Cardus, Departments of Rehabilitation and Physiology; and Dr. Vallbona, Departments of Rehabilitation, Physiology, and Pediatrics.

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SUMMARY

A review has been made of possible mechanisms of orthostatic intolerance to passive tilt, which includes observations from water immersion and bedrest experiments. The review relates the observation on cardiovascular function, intravascular volume, and transfer of fluids and electrolytes into and out of the vascular system to orthostatic intolerance to passive tilt. Experimental procedures are suggested which would test the meaning of the observations to account for the intolerance to passive tilting after prolonged bedrest.

INTRODUCTION

The effect of prolonged periods of weightlessness on various body functions is not fully known. There have been observations of orthostatic cardiovascular instability and dehydration in association with two relatively short duration orbital flights of the United States[1,2] to date.

Water immersion and bedrest immobilization experiments are believed to simulate some of the conditions of weightlessness. Information from such studies may be helpful to predict cardiovascular changes which can occur in association with space flight, and for interpretation of some of the observations made in association with an actual space flight. During water immersion[3,4,5,6,7,8,9] and bedrest[10,11,12,13] experiments there has been found a significant mobilization or redistribution of body fluids, as well as cardiovascular intolerance to passive tilt. Experimentation has also established a relationship of decreased work capacity and orthostatic cardiovascular changes to diminished blood volume.[14,15,16]

Of the three fluid compartments, the intravascular fluid compartment (blood volume) directly affects such aspects of cardiovascular performance as response to exercise or passive tilting. The effect is related not only to the volume of blood present, but also to the availability of this blood for return to the heart for filling and then delivery to the peripheral arterial system. The intravascular fluid compartment is of further importance in maintaining over-all fluid balance of the body. Fluids taken into the body are absorbed and pass into this compartment (for the most

part) to be transported to other fluid compartments of the body. This compartment also is intimately concerned with fluid elimination by both renal and insensible mechanisms. Electrolyte balance and rate of transfer between the various body fluid compartments also occur through the intravascular fluid compartment.

The following discussion on bedrest and water immersion studies relates the observations which have been reported in the literature on certain features of cardiovascular function, intravascular volume, and transfer of fluid and electrolytes into and out of the intravascular system. A possible mechanism accounting for some features of "cardiovascular deconditioning" is presented, and basic experimental procedures are suggested which would test the validity of this hypothesis.

REVIEW OF THE LITERATURE

Blood Volume:

Redistribution of the fluid in body compartments, resulting in orthostatic cardiovascular changes has been observed in both clinical and experimental circumstances. Thompson, et al.[17] in 1928, described variations in blood volume, measured by a dye dilution method, as a result of changes in the posture of his subjects. Circulating plasma volume was observed to decrease 12 per cent in rising from the recumbent to the erect position. This decrease occurred in 20 to 30 minutes. Upon resuming the recumbent position, it was noted that a much longer and variable period of time was required for the blood volume to return to the original value. Changes in volume also were associated with changes in hematocrit, plasma protein, and specific gravity of the blood, which suggested that the volume loss was constituted primarily of water and diffusible substances that filtered through capillary walls in the lower extremity. This process was considered to be a result of the increased hydrostatic pressure in these vessels when the erect position is assumed.

Waterfield,[18] in 1931, further evaluated the effect of rapid postural changes on the circulating blood volume, using a carbon monoxide method to measure blood volume. His results were in agreement with Thompson, in that he found an average plasma volume loss of 15 per cent upon assuming the erect position occurring over a 40 minute interval. Swelling of the legs was noted and was thought to result from the passage of plasma into the lymph spaces. In further studies by Waterfield,[19] reported in 1931, detailed observations of the effect of posture on the volume of the leg were reported. Changes in volume of the lower extremity up to the level of the tibial tuberosity were evaluated by use of a water displacement apparatus. By having the subject produce muscular contraction of the leg, an attempt was made to account for the contribution of the volume of the venous system of the leg to the total leg volume. Waterfield observed a swelling of 60 to 120 cc. in each lower extremity after a period of 40 minutes in the erect position. Voluntary muscular contraction did not result in volume differences that could be attributed to venous volume changes. Upon returning to the recumbent position, and over a similar period of time, there was return of approximately one-half of the observed volume change as

occurred in assuming the erect position, indicating that the return of the fluid to the circulation was slower than its exit. Waterfield observed further that if the subject exercised his legs before lying supine for 40 minutes, the total leg volume would be 120 cc. less than it was after standing stationary for 40 minutes. With exercise, there appeared to be an acceleration of the transfer of fluids back into the vascular system. It was noted further that volume changes in the leg were greatest in persons who were tall, in poor physical training, or had flabby legs.

Youmans[20] and co-workers noted an 18 to 40 per cent increase in serum protein concentration and a 29 to 65 per cent increase in colloid osmotic pressure of venous blood from the foot in healthy persons standing for 1 hour. The volume of the leg increased in the range of 3.11 to 4.87 cc. per 100 cc. of total volume. Calculations made by Youmans suggested that an increase in tissue pressure was three to five times as important in limiting loss of fluid components from the blood as was an increase in colloid osmotic pressure.

Fawcett[21] and associates, in 1960, studied the blood volume of patients with edema and low plasma protein concentrations. A larger fluid shift was noted in these patients as compared with a normal control group. This greater shift was attributed to a loss of plasma protein in the erect posture as a result of increased vascular permeability to protein. Upon returning to the recumbent position, the reversal of the observed changes was slower than occurred on assuming the erect posture.

Eisenberg,[22] in 1963, using a radioisotope technique to determine blood volume, confirmed the larger decrease in plasma volume that occurred with standing in hypoalbuminemic subjects (Laennec's cirrhosis). Decreases in plasma volume exceeded 20 per cent. This loss of plasma volume was well tolerated by the hypoalbuminemic subjects; this was attributed to an associated 35 per cent increase in blood volume found in individuals with cirrhosis.[23]

An increase in blood volume associated with relatively short periods of recumbency has been observed. Perera, et al.[24] observed serum protein concentration changes for different body positions. A fall in serum protein of 0.8 gram per 100 cc. was noted at night in recumbent patients who had been ambulatory during the day. It also was noted that the serum protein concentration did not rise during the day in patients confined to bed. The fall in protein level was interpreted to reflect increased plasma volume, which was offered as a possible mechanism in the etiology of paroxysmal dyspnea. Significant changes in serum protein concentration were found also to occur with walking for as short a period of time as 5 minutes.

Weiss and Robb[25] had previously suggested that patients with low plasma protein are more susceptible to severe attacks of paroxysmal dyspnea.

Iseri and associates[26] measured the RISA volume in compensated cardiac patients and confirmed the finding of a decreased plasma volume on standing. A

12.7 per cent decrease in plasma volume was noted with 30 to 50 minutes of standing. No change in plasma osmolarity and sodium concentration was noted, but total osmolar content of the plasma, determined from observed plasma volume and osmolar concentration, decreased significantly on standing. Two subjects were evaluated while standing in deep water; plasma volume (RISA space) in these subjects remained unchanged, but the blood hematocrit increased. Plasma osmolarity and plasma sodium were unchanged. The explanation for this discrepancy in hematocrit and RISA volume is unclear, and no indication is given of the volume of urinary output during this period of standing in the water. Nineteen patients in this study were required to exercise in air for 10 minutes, after which there was noted a 6 to 8 per cent decrease in plasma volume. In contrast to the effect of postural shifts, exercise produced a sharp rise in plasma osmolarity and sodium concentration. It was concluded that water was removed from the blood by exercising muscle tissue, and that the transfer was not a result of increased hydrostatic pressure within the capillaries which would force water and solutes into the interstitial space in proportionate quantities.

Widdowson and McCance[27] described the effect of bedrest on plasma volume as reflected by the hemoglobin concentration and hematocrit. A fall in hematocrit (increase in plasma volume) was noted after 1 or 2 hours of recumbency, and either a return of hematocrit to normal or a rise above control levels (decrease in plasma volume) was noted after 4 days of bedrest. The secondary rise of hematocrit (decrease in plasma volume) was attributed to a physical inactivity rather than recumbency. Cranson and Brown[28] evaluated plasma volume in both normal subjects and hypertensive patients and described a diurnal variation in plasma volume in both groups.

Using Evans' blue dye, Taylor et al.,[29] in 1945, evaluated the effect of bedrest on blood volume and pulse rate in response to exercise in normal young men. A 15 per cent decrease in plasma volume was noted after 3 weeks of bedrest. Acute changes in plasma volume which may occur upon resuming the upright position after bedrest were not evaluated. The subjects in this study were allowed to get out of bed daily for bathroom privileges. A correlation was not demonstrated between the chronic decrease in blood volume and the increase in resting pulse rate or poor postural adjustment.

Deitrick, Whedon, and Shorr[10,11] noted in four subjects a decline in plasma volume that ranged from 120 to 320 cc., with an average decrease of 191 cc., at the end of 3 weeks of immobilization. During the next 3 to 4 weeks of continued recumbency, the blood volume returned toward control levels. In one subject, who fainted rapidly on tests during immobilization, a greater increase in extravascular fluid (by leg circumference measurements) was noted to take place within 5 minutes of tilting after bedrest than had occurred in 13 to 20 minutes of tilting in the control period before bedrest.

Graveline and Jackson,[30] in water immersion experiments, showed a substantial increase in hematocrit at the end of the 6 hour test period, which implied a decrease in plasma volume with immersion. The hematocrit changes have been described in more detail in other studies,[5,31] and are as follows: a decrease in hematocrit (hemodilution) in 6 hour experiments, no changes in hematocrit in the 12 hour experiments, and an increase in hematocrit (hemoconcentration) in the 24 hour experiments. Hematocrits were performed after emersion from the water experiments. Graveline also described a marked increase in volume of urinary output, followed by thirst, in his experiments.

McCally[9] has measured blood volume changes during recumbency using radioisotope (RISA) techniques as well as from observations of the changes in hemoglobin and hematocrit. Using the hemoglobin and hematocrit values, he confirmed that there is an initial hemodilution followed by hemoconcentration as reported by Graveline. The values of blood volume obtained using RISA were not reported, and the author concluded that the method was not suitable for the study of rapid blood volume changes.

Other studies have been directed to evaluating circulatory changes due to loss of whole blood rather than plasma. Here the clinical implication is much more pronounced. Because of the extensive amount of literature, no attempt will be made to make a complete survey.

Green and Metheny[14] have described the use of the tilt test to assess acute blood loss from bleeding. The manifestations of increased heart rate and decreased blood pressure noted in this circumstance closely resemble those seen in bedrest immobilization. Balke et al.[15] have evaluated work capacity after blood donation, and noted reductions in optimal work capacity. Gullbring and associates[16] have studied the effect of bleeding and retransfusion on pulse rate in the supine and upright positions and during exercise, and have demonstrated orthostatic changes in heart rate and blood pressure after venesection.

The effects of exercise on blood volume are not conclusive. Observations appear to have been limited to the study of acute changes in blood volume after short bouts of exercise. Under these circumstances both increases[32,33] and decreases[34,35,36] in blood volume have been reported. The effect of repeated short periods of exercise in association with prolonged bedrest cannot be inferred from the studies listed above.

Urine Volume and Urine Electrolyte Excretion:

A decrease of urine flow and sodium excretion is known to occur in changing from the recumbent to the erect position. Changes from the erect to the recumbent position result in opposite effects. Such a decrease in urine volume and sodium excretion is not found in assuming the erect position in water. In fact, many of the changes that occur with water immersion appear to be an

exaggeration of the changes noted upon assumption of the recumbent position in air. For this reason, water immersion will be compared to bedrest, and will be discussed in this section.

Bazett[37,38] noted a diuresis to be associated with water immersion. He thought that the diuresis resulted from a transfer of fluid from the interstitial spaces of the legs to the blood space, and thence to the urine. This report showed that recumbency alone resulted in increased urine flow; and that immersion up to the neck, in a semi-reclining position, also resulted in an increased urine flow. Bazett thought that a dilation of the splanchnic vessles, rendered possible by changes from the vertical position, altered renal circulation and improved intestinal absorption. This, he thought, explained the changes that result with both recumbency and water immersion. Bazett did not observe diuresis when only the extremities of the subject were immersed, but did observe diuresis when the entire body was immersed. The position of the subjects maintained in immersion of the extremities was not indicated. In their studies, Bazett et al.[38] also noted an increase of the hemoglobin (hemoconcentration) in the immersion situation, and described a decrease (hemodilution) if only a recumbent position was maintained.

Epstein and associates[39] found that diuresis occurred in the erect as well as recumbent position in water. The mechanism of this diuresis and possible changes in body fluid compartments with water immersion is probably more complicated than found in bedrest.

Graveline[31] also has described cardiovascular intolerance to tilting to the upright position after prolonged periods of water immersion, and further indicated a "protective effect" by intermittently obstructing venous return of the extremities using a tourniquet technique. He also mentioned bedrest experiments performed by him which resulted in tilt table cardiovascular intolerance, and indicated that strenuous daily exercises of the sit-up and push-up variety were not helpful in maintaining cardiovascular adaptability.

Graveline and McCally[40] have described a fourfold increase in urine flow, a twofold increase in urea output, and a sixfold increase in sodium excretion with water immersion. It was noted that the administration of pitressin returned urine flow rates and solute excretion to control levels. This suggested that the increased flow was due to antidiuretic hormone (ADH) inhibition. Graveline, et al.[4] described a marked elevation in nitrogen excretion in the urine during the first 3 days of water immersion, which corresponded closely to the polyuria noted. Graveline and Barnard[5] further noted a diurnal variation in urinary specific gravity, probably related to the known nocturnal increase in ADH.[41,42,43] They also described an intense thirst accompanying the diuresis observed.

Beckman[44] observed a similar diuresis with water immersion. This group[45] later did not substantiate the same marked diuresis or urinary dilution with an 18 hour period of immersion, when a slightly positive intrapulmonary pressure was established during expiration.

Positive pressure breathing has been described[46] to result in a decreased urinary output. Brown, et al.[47] in an effort to explain the hemoconcentration found in the last stages of labor, found that repeated positive pressure maneuvers (Valsalva maneuvers) resulted in a decrease in plasma volume. It is known that a decrease in plasma volume is associated with a decrease in urine flow, which perhaps could partially or totally explain the failure of Beckman's group to observe a diuresis with water immersion.

Gauer and associates[48] showed that negative pressure breathing produced a marked diuresis, the opposite effect to that seen with positive pressure. Boylan and Antkowiak[49] have shown that negative pressure breathing is not accompanied by a decrease in plasma osmotic pressure. A possible mechanism of this diuresis is suggested by Henry, et al.,[50] who showed that distention of the left atrium with a balloon results in a marked diuresis, and that the response to negative pressure breathing is changed by section of the vagus nerve in dogs. This response can be blocked also with vasopressin.[49,51]

A similar atrial stretch receptor has been demonstrated by Anderson and his group,[52] who found significant reductions in secretion of aldosterone with right atrial stretching, but not with left atrial stretching. Gourenlock[53] and associates evaluated urine aldosterone excretion in subjects who stood for 3 hours following 2 hours of recumbency. Increased urinary aldosterone levels were observed in the subjects who stood in air, and a fall in aldosterone in subjects who remained recumbent or stood in water. Urinary sodium loss decreased on standing in air, and was unaltered by continued recumbency or standing in water.

Thomas[54] has observed reductions in both urinary flow and sodium excretion in subjects who stood after several hours of recumbency, and described opposite changes upon lying down. The duration of the experiments after a change in posture was approximately 3 hours.

In an effort to explain the mechanism of these types of observations, Epstein[55] stresses the importance of glomerular filtration and renal blood flow in relation to sodium excretion by the kidney. He described a concept of a "volume" receptor (of the type implied in the discussion above) as having an appeal which is "seductive and too easily verablized."

Welt[56] states, "There are undoubtedly many mechanisms that influence the excretion or retention of salt, and thereby control the volume of body fluids within narrow limits." He discussed four mechanisms: 1) basic mechanisms which are intrinsic to the kidney itself, 2) neural regulatory mechanisms, 3) hormonal influences of aldosterone, and 4) effects of a natruretic hormone.

Smith[57] has reviewed the subject of water and electrolytes and summarized his findings. He described three methods for inducing diuresis without an apparent decrease in osmotic pressure of the blood as follows: 1) isotonic saline administered in the supine position, 2) iso-oncotic albumin in saline, and

3) negative pressure respiration. He further described three mechanisms that result in antidiuresis with an apparent increase in osmotic pressure as: 1) orthostasis, 2) venous occlusion, and 3) hemorrhage. He further recognized the central mechanism of water control through ADH and its osmoreceptor system, as well as the osmotic diuresis which exerts an inhibitory effect on water reabsorption by the renal tubules.

In commenting on sodium excretion, Smith states that neither ADH, nor total body water plays a direct (regulative) role in sodium balance. He noted that sodium excretion may be increased immediately upon assuming the supine position, but he thinks such postural natruresis is transient, and interprets it merely as reflecting the antinatruretic state activated by the antecedent orthostasis. Supporting experimental data are not presented.

In contrast, Berliner[58] summarizes the regulation of sodium excretion as follows:

> "Because the sodium salts constitute all but a very small fraction of the solute of extracellular fluid, the sodium concentration varies with the osmotic pressure of plasma. Since the osmotic pressure is regulated by the excretion and retention of water, it follows that the concentration of sodium in the plasma is regulated through the control of water excretion and not by the modulation of sodium excretion. It also follows that the amount of sodium in the extracellular fluid bears no relation to its sodium concentration; the latter reflects osmotic pressure. Since the osmotic pressure is maintained within rather narrow range, the amount of sodium in the extracellular fluid, and hence in the body is related more closely to the extracellular fluid volume. It would be anticipated, therefore, that sodium excretion should be modulated in relation to the volume of extracellular fluid, and this appears to be the case, although in what fashion this regulation is achieved remains uncertain. The rate of sodium excretion of course is determined by the balance between filtration and reabsorption, but each of these is varied and regulated in a way which cannot yet be subjected to detailed analysis."

He comments further as follows:

> ".... Thus, although the ion exchange immediately suggests the excretion of sodium and potassium should vary inversely, the reverse is more often true, increasing the sodium delivered to the mechanism (most of which remains unabsorbed and is, therefore, excreted) enhances potassium excretion under many conditions."

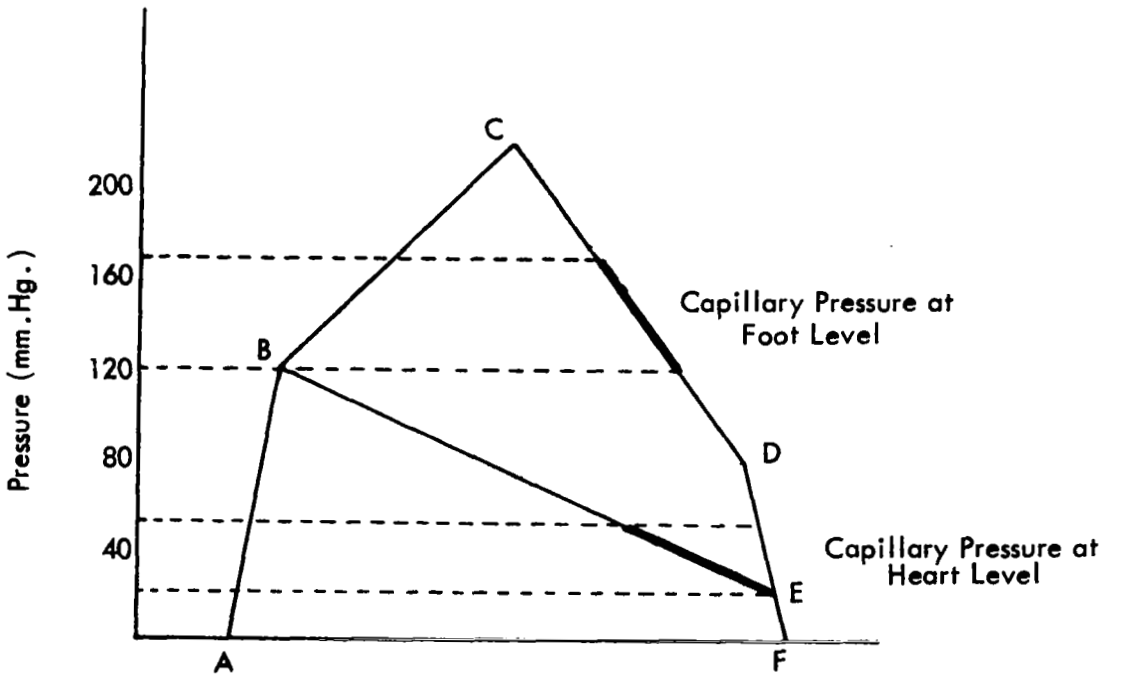
DISCUSSION

The ability of man to adapt to rapid changes in posture probably results from a combination of factors. An increase in heart rate and arteriolar constriction[59] occur to maintain blood pressure that would otherwise fall because of a diminished stroke volume in the upright position. The maintenance of adequate return of blood to the heart for distribution to the peripheral arterial system also contributes to preservation of cardiac function in the upright position.

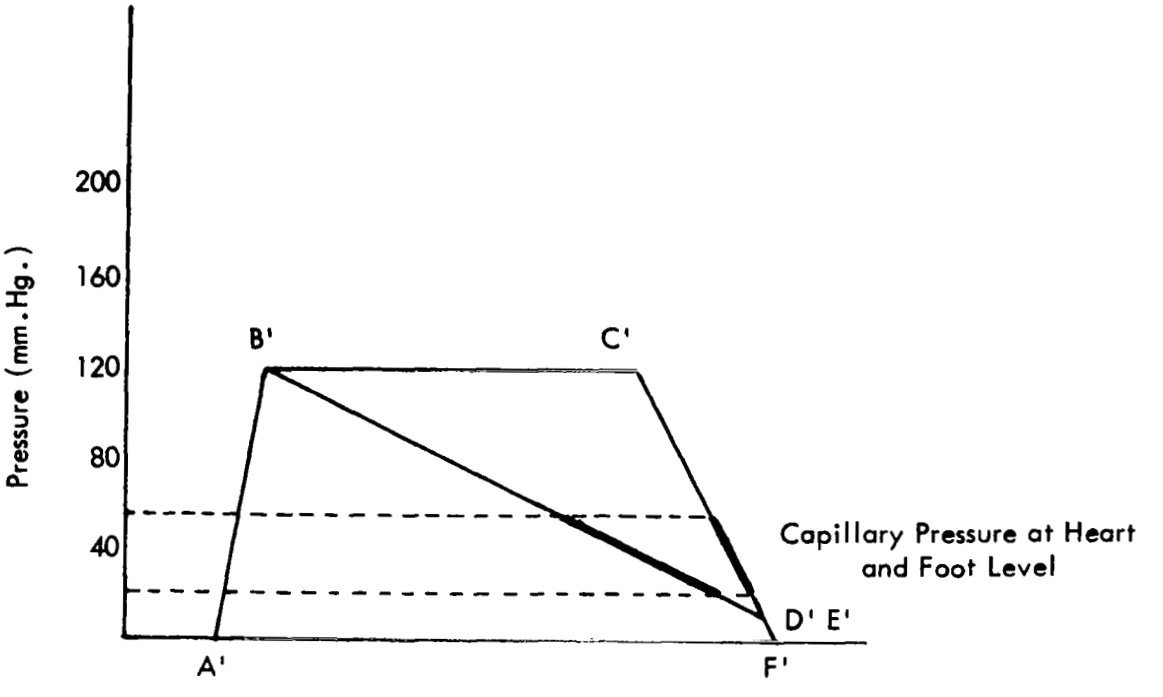
When man assumes the erect position, the vascular fluid columns of the body are subjected to a head-to-foot line of gravitational force. Thus, the weight of the vertical fluid column of the vascular system produces a large hydrostatic pressure force in the lower extremity. Pooling of blood in the leg veins, and a transfer of fluid from the intravascular space, under the effect of this pressure can result in a decreased volume of venous blood returned to the heart unless fully compensated by an increase in venous pressure. Several mechanisms operate to compensate for, or to overcome, the changes that result from standing.

In standing, there is an effective venous pressure in the ankle of approximately 85 mm. Hg.[61] Since the venous system is considered to be a low pressure system, it would seem that this gradient of pressure would limit return of blood to the heart. But, in the standing position, the weight of the column of blood in the arterial and venous systems exerts a similar pressure effect at the foot level. The gradient of pressure from the arterial circulation to the venous system is approximately the same for all anatomical sites. However, the effect of the weight of the column of blood in producing a hydrostatic pressure force should increase the capillary pressure at the foot and lower leg and produce a greater transfer rate of fluid and solutes out of the capillary into the extravascular spaces. This transfer of fluids should continue until tissue pressure and other factors affecting transfer balances the increased intracapillary pressure effect. A comparison of the pressure gradients and mean pressures of the cardiovascular system for the recumbent and upright positions are shown diagramatically in Figure 1.

The upper diagram shows the pressure gradients that occur in the vascular system in the erect position. The pressure difference between points A and B represents that force produced by the contraction of the heart. The increase in pressure between B and C results from the action of gravity on the fluid column of the arterial system, with the point C representing the arterial pressure in the foot. C and D represent the arterial-venous pressure difference. There is a corresponding action of gravity on the venous fluid column such that the venous pressure in the foot would be represented by the pressure at point D. Point E represents the venous pressure at the input to the heart, and point F represents the lowest pressure in the heart. The capillary pressure is somewhere between the arterial and venous pressures depending on the arteriolar and venous vessel caliber.



a) Pressure Gradient in Erect Position



b) Pressure Gradients in Recumbent Position

Figure 1. Cardiovascular pressure gradients for erect and recumbent positions.

The lower diagram represents the pressures at the same anatomical location in the recumbent position. C' and D' represent the arterial-venous pressure differences. In both the recumbent and erect position, the arterial-venous pressure difference is approximately the same, but in the erect position (upper figure) the capillary pressure in the dependent portion of the body is markedly elevated, the elevation being dependent on the fluid column height above the capillary site. Such hydrostatic pressure forces would not occur in space flights where there is zero gravity.

Increased capillary hydrostatic pressure should tend to cause fluid and electrolytes to transfer out of the vascular space into the interstitial space. In addition, the increased hydrostatic pressure tends to produce venous dilation and pooling, depending upon venomotor tone. Some of the loss of plasma volume to the extremities is compensated for by a shift of blood from the thoracic compartments. The pumping action of muscles provides some assistance in returning available venous blood to the heart. Muscular contraction may also be of importance in expediting the transfer of interstitial fluid back into the intravascular space by raising tissue pressure.

Schematically presented in Figure 2 are the various pressures that are important in transfer of fluid to and from the intravascular compartment. The colloidal osmotic pressure of the plasma proteins is shown as Pi and Po for that which occurs intravascularly and extravascularly, respectively. The net colloidal osmotic pressure is approximately 30 mm. Hg. In addition there is an extravascular tissue pressure, I, that tends to prevent transfer of fluid out of the vessels. Upon assuming the erect position, the resultant force (net force vector) acts to transfer fluid out of the vascular space. The hydrostatic fluid pressure, resulting from the effect of a gravity vector acting parallel to the long axis of the body thus tends to force fluids out of the vascular system. The large variation in capillary pressure magnitude produced as a result of gravity force suggests it is a potent factor in body compartmental shifts of fluid.

Normally, there is not a free exchange of the protein fraction of blood into the extravascular space. Loss of the plasma water thus results in a compensatory increase in net colloidal osmotic pressure, although the magnitude of this change is probably not very large. The transfer of the fluid to the extravascular space results in a rise in extravascular tissue pressure because of the confinement of the skin and supporting tissue.[62] The extravascular pressure usually would increase with small changes in volume of this space, since it occupies an expandable, but limited volume. The degree of expansion of this volume may differ in extremities with alterations in ratio of fat, muscle, and other tissue components. Soft flabby tissue could accommodate a larger volume of fluid accumulation in the extravascular space. The role of vascular permeability is also important, especially in disease states.[22,23]

It is suggested that venous pooling and transfer of fluids to the extravascular space represent two of the potent mechanisms accounting for orthostatic cardiovascular responses after bedrest.

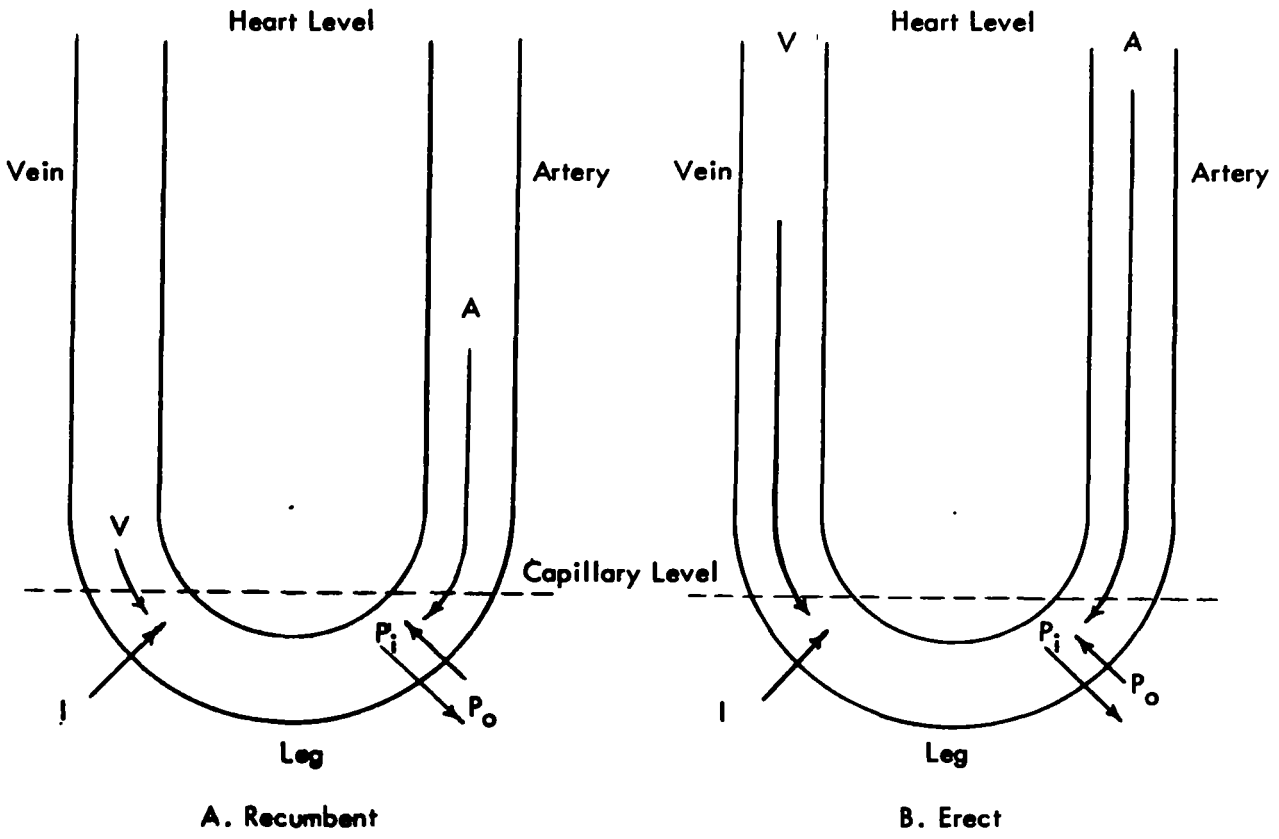


Figure 2. Pressure important in transfer of fluids across vascular wall.

V = Venous pressure
A = Arterial pressure
I = Interstitial pressure
P_i = Colloidal osmotic pressure outside vessel
P_o = Colloidal osmotic pressure in vessel

During prolonged bedrest, with the removal of the effect of hydrostatic pressure force produced by gravity, there should result a relatively slow transfer of extravascular fluid of the legs to the vascular system, thence to the thoracic or abdominal pools, and finally out of the body by urine or insensible fluid losses. This transfer of fluid can account for some of the diuresis observed with bedrest immobilization.

A diminished interstitial fluid volume should result from the loss of this fluid, and should be shown by a decrease in circumference of the legs, if composition of the tissues otherwise did not change. Upon assuming the erect position after bedrest, the net force vector for transfer of fluid out of the vascular system again is suddenly greater. Because the expandable extravascular space is reduced to minimal volume during bedrest, relatively more fluid shift is possible before there is a build-up of interstitial pressure to equalize fluid transfer. There is thus a possible magnification of changes which occurs before bedrest. In addition, if there is also a diminished blood volume due to prolonged bedrest, this would summate with the above effects and exaggerate orthostatic cardiovascular responses.

The rate of transfer of fluid out of the vascular space in assuming the erect position is rapid, occurring in minutes. This, too, may account for the downward trend of mean blood pressure noted during passive tilting of subjects after prolonged bedrest. The changes in heart rate and blood pressure immediately after tilting probably reflect a physiological response to a greater degree of venous pooling than occurs as a result of loss of venomotor tone during prolonged bedrest. Lack of muscular exercise during recumbency could contribute to this decreased venomotor tone.

To test this hypothesis, bedrest experiments first should be performed on a group of healthy subjects to determine their individual cardiovascular response to bedrest. Later, after recovery of normal response, the same group of subjects should be evaluated with bedrest in which controlled exercise and/or intermittent venous occlusion procedures are added. Tilt table and ergometry studies before and after bedrest should provide quantitative expressions of the cardiovascular changes that result from bedrest. Blood volume, fluid and electrolyte balances, and body weight changes should be studies. Hemoglobin and hematocrit changes and measurements of cardiovascular function (i.e., heart rate, blood pressure, body fluid compartment measurements, etc.) should be studied in detail during passive tilting. Leg volume or circumference measurements should be made both during the course of bedrest and at the time of tilt procedures. An evaluation should be made of pressure garments on the lower extremity, or of a partial body G-suit, to evaluate their value in controlling the orthostatic cardiovascular intolerance produced by bedrest.

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